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Case Report

A case of neurobrucellosis detected during brucella treatment

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Abstract
Brucellosis is a systemic zoonotic infectious disease caused by the gram-negative Brucella bacteria that can be transmitted from infected animals to humans. Neurobrucellosis occurs when the central nervous system is directly or indirectly affected by Brucella spp. Clinical meningoencephalitis in neurobrucellosis includes meningovascular involvement, parenchymal dysfunction, peripheral neuropathy/radiculopathy, and various degrees of behavioral abnormalities. At the admission of our case, psychiatry was consulted considering psychosis due to decreased speech and agitation, there were no signs of meningeal irritation in physical examination, and no cells were seen in the first CSF examination. In the presence of unexplained neurological and psychiatric symptoms, especially in endemic areas, neurobrucellosis should be considered in the differential diagnosis, and necessary blood and CSF tests should performed.

Keywords
Meningoencephalitis; Brucellosis; Neurobrucellosis

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Introduction

Brucellosis is a systemic zoonotic infectious disease caused by the gram-negative Brucella bacteria that can be transmitted from infected animals to humans. It is the most common zoonotic disease in the world and is an important public health problem in many developing countries. Brucella can affect any organ or system, and the disease manifests in many different clinical forms. Neurobrucellosis occurs when the Central Nervous System (CNS) is directly or indirectly affected by Brucella spp. (available at: https://www.uptodate.com/contents/brucellosis-epidemiology-microbiology-clinical-manifestations-and diag nosis?search=brucella&source=search_result&selectedTitle=1~104&usage_type=default&display_rank=1.) Neurological involvement rate can be seen in 0-25% of brucellosis cases [1]. The clinical spectrum of neurobrucellosis is very heterogeneous. Neurological manifestations in neurobrucellosis can be seen in the acute or late stages of the disease. In the clinic, it can be seen as acute/chronic meningitis, meningoencephalitis, brain abscess, myelitis, radiculitis and/or neuritis (cranial or peripheral nerve involvement). Although the incidence of CNS involvement is not high, it may result in serious morbidity [2]. Neurobrucellosis may present with different clinical presentations and its diagnosis may be difficult. Therefore, we aimed to draw attention to this complication with our case.

Case Report

A nineteen-year-old male patient was brought to the emergency room by his relatives with complaints of sudden onset of vomiting, meaningless speech, and decreased speech, was evaluated by a psychiatrist in the emergency room and no psychiatric illness was considered. Although demyelinating and vasculitic diseases were considered in the differential diagnosis in the patient evaluated by a neurologist, consultation with an infectious diseases specialist was recommended in terms of central nervous system infection. The patient was evaluated in the emergency room, and it was learned that he had complaints of sudden onset of vomiting and impaired speech. It was learned that the patient applied to the urology outpatient clinic 8 months ago due to fever and unilateral orchitis, and that the brucella tube test was negative at that time, brucella was not considered, but the patient was diagnosed with brucellosis 5 months later, as complaints of fatigue and joint pain continued. It was learned that the patient had been using rifampicin 1x600 mg tb and doxycycline 2x100 mg tb for 3 months. It was found that the patient regularly used his drugs. From the history of the patient, it was found that he lived in the village and was engaged in animal husbandry.

On physical examination, he was conscious, partially cooperative, and disoriented. His speech was reduced, his interest in the environment was low, his attention was reduced, he had meaningless speech and aggression. There were no signs of meningeal irritation. Other system reviews were normal. There were no signs of acute bleeding or edema in the cranial tomography. Cranial diffusion magnetic resonance imaging (MRI) did not show signs of acute ischemia, and cranial MRI findings showed plaque appearances consistent with bilateral demyelinating/vasculitic lesions in the white matter (Figures 1, 2). The patient underwent lumbar puncture (LP) in the emergency. No leukocytes were seen in the cerebrospinal fluid (CSF) examination. CSF protein was 295 mg / dL (15-45), CSF glucose was 2.5 (45-80 mg / dL), concurrent blood glucose (sour blood sugar) was 111 mg / dL.

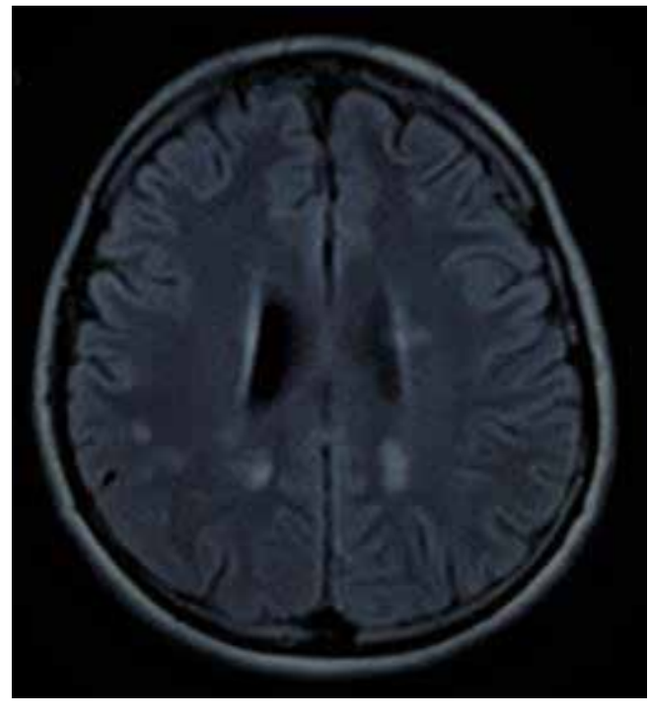

Figure 1. Ischemic/demyelinating lesions in bilateral periventricular white matter in MRI flair axial sections

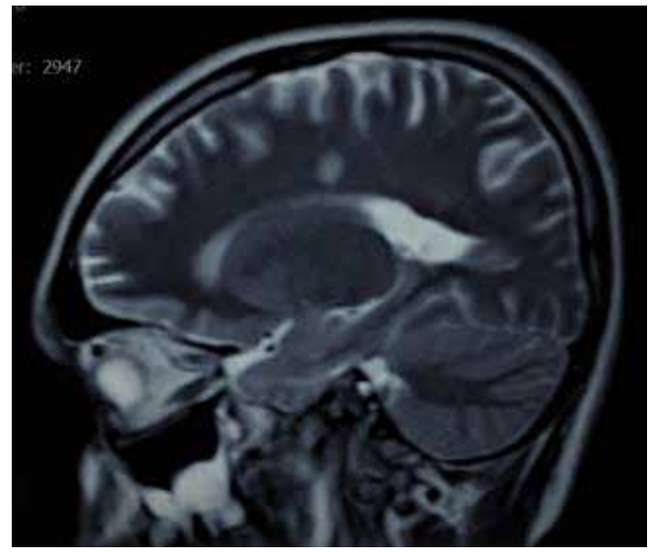

Figure 2. MRI T2 sagittal section ischemic/demyelinating lesion perpendicular to the corpus callosum

The patient was started with ceftriaxone 2x2 gr IV, vancomycin 2x1 gr IV, acyclovir 3x750 mg iv with the diagnosis of meningoencephalitis, and she was taken to the neurology intensive care unit. No features were found in the CSF Gram and ARB staining of the patient. CSF mycobacterium polymerase chain reaction (PCR) was negative, there was no growth in mycobacterial culture. Herpes simplex virus 1 and 2, human parechovirus, enterovirus, mumps and varicella zoster virus were found negative in the CSF viral meningitis panel. There was no reproduction in the CSF and blood culture. In brucella agglutination tests in CSF fluid and blood, neurobrucellosis was

considered in the patient because of positive findings in CSF with a titer of 1/640 and above and a titer of 1/320 in the blood. Treatment was continued with ceftriaxone, rifampicin and doxycycline. The cooperation and orientation of the patient improved with the treatment. It was detected in 40 cells/mm3 in LP performed on the 21st day of treatment, it was 75% lymphocytes. CSF protein was found to be 124 mg/dL, CSF glucose 32, and concurrent blood glucose 103 mg/dL. Ceftriaxone treatment was completed within 1 month, and the patient was discharged with rifampicin and doxycycline treatment. At the end of the first month of the follow-up, the patient had no complaints, his physical examination was normal. The treatment of the patient was completed for 6 months.

Discussion

Clinical meningoencephalitis in neurobrucellosis includes meningovascular involvement, parenchymal dysfunction, peripheral neuropathy/radiculopathy and various degrees of behavioral abnormalities [1]. It can be confused with chronic central nervous system infections or with migraine, convulsion, hemiplegia, temporary parkinsonism, tremor, general rigidity, psychosis and neurosis [3]. Several behavioral and neuropsychiatric diseases, sleep disorders, epilepsy, agitation and depression have been detected in patients with neurobrucellosis. The recovery of cognitive and mood disorders in brucellosis without treatment with antidepressant and/or antipsychotic distinguishes the disease from functional psychiatric diseases [4,5]. Similarly, in our case, psychiatry was consulted, considering it psychosis due to decreased speech at admission, lack of interest and attention to the environment, meaningless speech and aggression, and an increase in anxiety in the last 3 months.

It was stated that the clinical picture of neurobrucellosis can be variable, and the findings are not specific, therefore, CSF examination can be more helpful in making the diagnosis [1,4]. The diagnosis of neurobrucellosis can be made with the presence of a neurological picture that cannot be explained by another neurological disease, isolation of bacteria in the CSF or blood culture, or positivity in serological tests, abnormal CSF findings (low CSF glucose, increased CSF protein, lymphocytic pleocytosis) [3-5]. The low bacterial isolation rate in the CSF (5-30%) necessitates the use of serological diagnostic methods in most of the patients [1,4]. Similarly, in our patient, serologically positive blood and CSF were detected, but bacteria could not be isolated in the CSF and blood culture.

There are four imaging findings in the radiological diagnosis of neurobrucellosis: normal, inflammation (meningeal enhancement), white matter changes and vascular changes. In a study conducted in Turkey, 263 neurobrucellosis cases were evaluated, 54.3% had normal MRI findings, the most common changes were leptomeningeal (n = 44) and basal meningeal involvement (n = 30), white matter involvement with demyelinating lesions (n = 32), chronic cerebral ischemic changes are vascular involvement (n = 37) and brain edema (n = 40) [6].

There is no consensus on antibiotic choice, dose and duration in the treatment of neurobrucellosis. Double or triple combination therapy with doxycycline, rifampicin, trimethoprim-sulfamethoxazole, streptomycin or ceftriaxone is recommended [5]. In a study conducted in Turkey, it is recommended to continue with ceftriaxone, doxycycline and rifampicin after 1 month of treatment, and doxycycline and rifampicin, treatment with ceftriaxone was found to be more successful in terms of relapse and treatment failure compared to other treatment options, and it was shown that the treatment duration was shorter compared to oral treatments [2]. Clinical response and normalization of CSF findings are the main factors that determine the duration of treatment [1]. Our patient received treatment for uncomplicated brucellosis, used his medications regularly, but the disease was complicated with neurobrucellosis, so no response was obtained with the current treatment. Following the addition of ceftriaxone for neurobrucellosis, a clinical response was obtained, while doxycycline and rifampicin treatment was extended for 6 months.

As a result, the clinical spectrum of neurobrucellosis is highly variable. At the admission of our case, psychiatry was consulted considering psychosis due to decreased speech and agitation, there were no signs of meningeal irritation in physical examination, no cells were seen in the first CSF examination. In the presence of unexplained neurological and psychiatric symptoms, especially in endemic areas, neurobrucellosis should be considered in the differential diagnosis, and the necessary blood and CSF tests should be performed.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Yetkin MA, Bulut C, Erdinç FŞ, Oral B, Tulek N. Evaluation of the clinical presentations in neurobrucellosis. Int J Infect Dis. 2006; 10(6):446-52.

2. Erdem H, Ulu-Kilic A, Kilic S, Karahocagil M, Shehata G, Eren-Tulek N, et al. Efficacy and tolerability of antibiotic combinations in neurobrucellosis: results of the Istanbul study. Antimicrob Agents Chemother. 2012; 56(3):1523-8.

3. Ural O, Güler S. Nörobruselloz: Bir Olgu Nedeniyle (Neurobrucellosis: Due to a Case). Flora Dergisi. 2007; 12(4):208-10.

4. Gul HC, Erdem H, Bek S. Overview of neurobrucellosis: pooled analysis of 187 cases. Int J Infect Dis. 2009; 13(6): e339-43.

5. Guven T, Ugurlu K, Ergonul O, Kocagul Celikbas A, Eren Gok S, Comoglu S, et al. Neurobrucellosis: clinical and diagnostic features. Clin Infect Dis. 2013; 56(10):1407-12.

6. Erdem H, Senbayrak S, Meriç K, Batirel A, Karahocagil MK, Hasbun R, et al. Cranial Imaging Findings in Neurobrucellosis: Results of Istanbul-3 Study. Infection. 2016; 44(5):623-31.

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